NATIONAL CANCER INSTITUTE
Technology Transfer Center

Gene Therapy for Treatment of CRX-Autosomal Dominant Retinopathies

Summary

The National Eye Institute (NEI) seeks research co-development partners and/or licensees for gene therapy for CRX retinopathies such as Leber congenital amaurosis, retinitis pigmentosa, and cone-rod dystrophy.

NIH Reference Number

E-008-2020

Product Type

- Therapeutics

Keywords

- Gene Therapy, NEI, Retinopathies, Leber Congenital Amaurosis, LCA, Retinitis Pigmentosa, RP, Cone-rod Dystrophy, CRD, Rare Disease, Adeno-Associated Virus, AAV, Lentivirus, Swaroop

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Mutations in the cone rod homeobox (CRX) transcription factor lead to distinct retinopathy phenotypes, including early-onset vision impairment in dominant Leber congenital amaurosis (LCA). Adeno-Associated virus (AAV) vector-mediated delivery of a CRX cDNA under the control of a CRX promoter region partially restored photoreceptor phenotype and expression of phototransduction genes in an in vitro model of CRX-LCA. Gene therapy using the CRX-AAV vector to retinal organoids derived from induced pluripotent stem cells (iPSCs) of a patient with the dominant CRX-I138fs mutation partially restored expression of visual opsins and other phototransduction genes as revealed by immunohistochemistry and single cell RNA-sequencing. Retinal organoids from iPSCs of a second dominant CRX-LCA patient carrying a K88N mutation also revealed loss of expression of opsins and phototransduction genes as a common phenotype, which could be alleviated by AAV-

mediated overexpression of CRX.

Potential Commercial Applications

- Early onset blindness, including Leber congenital amaurosis
- Gene therapy of CRX retinopathies; i.e., patients with a mutation in the CRX gene

Competitive Advantages

- Promising commercial potential given that there are no current treatments for CRX-retinopathies
- Gene therapy by delivering CRX should restore photoreceptor structure and function
- Existing commercial interest and an established regulatory path for directly administered gene therapy targeting an ophthalmic disease caused by mutations in a specific gene: In 2017, Luxturna (voretigene neparvovec-rzyl) was FDA approved for an inherited form of vision loss (confirmed biallelic RPE65 mutation-associated retinal dystrophy) that may result in blindness

Inventor(s)

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Development Stage

- Discovery (Lead Identification)

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/962,732, Filed 17 Jan 2020

Therapeutic Area

- Eye and Ear, Nose & Throat

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